1072021 101694157 Page 1 7 12/15/02 4 1624

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L1 STRUCTURE UPLOADED

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L1 HAS NO ANSWERS

L1 STR

G1 Cb, Hy

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=> s l1 sss full FULL SEARCH INITIATED 09:53:18 FILE 'REGISTRY' FULL SCREEN SEARCH COMPLETED - 113987 TO ITERATE

100.0% PROCESSED 113987 ITERATIONS

1214 ANSWERS

SEARCH TIME: 00.00.03

L2 1214 SEA SSS FUL L1

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SINCE FILE TOTAL ENTRY SESSION

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FULL ESTIMATED COST

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FILE COVERS 1907 - 14 Dec 2004 VOL 141 ISS 25 FILE LAST UPDATED: 13 Dec 2004 (20041213/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> s 12

.3 10 L2

=> d 13 fbib hitstr abs total

- L3 ANSWER 1 OF 10 CAPLUS COPYRIGHT 2004 ACS on STN
- AN 2003:58083 CAPLUS
- DN 138:122660
- TI Preparation of piperazine oximes as neurokinin NK-1 receptor antagonists
- IN Van Maarseveen, Jan H.; Van Scharrenburg, Gustaaf J. M.; Tulp, Martinus Th. M.; McCreary, Andrew C.; Iwema Bakker, Wouter I.; Coolen, Hein K. A. C.; Herremans, Arnoldus H. J.; Van den Hoogenband, Adrianus
- PA Solvay Pharmaceuticals B.V., Neth.
- SO PCT Int. Appl., 39 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

t. MM.	CNI	- .																
	PAT	CENT :	NO.			KIN	D	DATE		APPLICATION NO.						DATE		
							-									-		
ΡI	WO	2003	0064	59		A1		2003	0123	1	WO 2	002-	EP74	72		2	0020	703
		W:	ΑE,	AG,	AL,	AM,	ΑT,	AU,	AZ,	BA,	BB,	BG,	BR,	BY,	ΒZ,	CA,	CH,	CN,
			CO,	CR,	CU,	CZ,	DE,	DK,	DM,	DZ,	EC,	EE,	ES,	FI,	GB,	GD,	GE,	GH,
			GM,	HR,	HU,	ID,	ΙL,	IN,	IS,	JP,	KE,	KG,	KP,	KR,	KZ,	LC,	LK,	LR,
			LS,	LT,	LU,	LV,	MA,	MD,	MG,	MK,	MN,	MW,	MX,	MZ,	NO,	NZ,	OM,	PH,
			PL,	PT,	RO,	RU,	SD,	SE,	SG,	SI,	SK,	SL,	ТJ,	TM,	TN,	TR,	TT,	TZ,
			UA,	ŪĠ,	US,	UZ,	VN,	YU,	ZA,	ZM,	ZW,	AM,	ΑZ,	BY,	KG,	KZ,	MD,	RU,
			ТJ,	TM														
		RW:	GH,	GM,	KΕ,	LS,	MW,	MZ,	SD,	SL,	SZ,	TZ,	ŪĠ,	ZM,	ZW,	ΑT,	BE,	BG,
			CH,	CY,	CZ,	DE,	DK,	EE,	ES,	FI,	FR,	GB,	GR,	IE,	IT,	LU,	MC,	NL,
			PT,	SE,	SK,	TR,	BF,	ВJ,	CF,	CG,	CI,	CM,	GA,	GN,	GQ,	GW,	ML,	MR,
			NE,	SN,	TD,	TG												
							`]	EP 2	001-	2026	31		A 2	0010	709
					A1		2004	0414]	EP 2	002-	7848	38		2	0020	703	

AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK A 20010709 EP 2001-202631 WO 2002-EP7472 W 20020703 20020703 BR 2002010080 20040622 BR 2002-10080 20010709 EP 2001-202631 20020703 WO 2002-EP7472 T2 20041209 JP 2003-512231 20020703 JP 2004536851 20010709 EP 2001-202631 WO 2002-EP7472 20020703 20031212 US 2004176389 **A1** 20040909 US 2003-480542 20010709 EP 2001-202631 WO 2002-EP7472 20020703

OS MARPAT 138:122660

IT

489437-44-7P 489437-45-8P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of piperazine oximes as neurokinin NK-1 receptor antagonists) 489437-44-7 CAPLUS

RN 489437-44-7 CAPLUS
CN Piperazine, 1-[3,5-bis(trifluoromethyl)benzoyl]-4-[[4,5-dihydro-5-(4-morpholinylmethyl)-1,2-benzisoxazol-3-yl]methyl]-2-(1H-indol-3-ylmethyl)-,
(2R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 489437-45-8 CAPLUS

CN Piperazine, 1-[3,5-bis(trifluoromethyl)benzoyl]-4-[[4,5-dihydro-5-(4-morpholinylmethyl)-1,2-benzisoxazol-3-yl]methyl]-2-(1H-indol-3-ylmethyl)-, monohydrochloride, (2R)- (9CI) (CA INDEX NAME)

● HCl

IT 489437-59-4P 489437-60-7P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation of piperazine oximes as neurokinin NK-1 receptor antagonists)

RN 489437-59-4 CAPLUS

CN Piperazine, 1-[3,5-bis(trifluoromethyl)benzoyl]-2-(1H-indol-3-ylmethyl)-4-[3-(2-methyl-1,3-dioxolan-2-yl)propyl]-, (2R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 489437-60-7 CAPLUS

CN Piperazine, 1-[3,5-bis(trifluoromethyl)benzoyl]-4-[2-(1,3-dioxol-2-yl)ethyl]-2-(1H-indol-3-ylmethyl)-, (2R)- (9CI) (CA INDEX NAME)

GI

$$\begin{array}{c|c}
X & R^2 \\
N & R^4
\end{array}$$

Title compds. [I; X = Ph, pyridyl substituted with 1-2 Me, CF3, OMe, halo, cyano, 5-CF3-tetrazol-1-yl; Y = 2- or 3-indolyl, Ph, 7-azaindol-3-yl, 3-indazolyl, 2-naphthyl, 3-benzo[b]thiophenyl, 2-benzofuranyl, which may be substituted with ≥1 halo or alkyl; n = 0-3; m = 0-2; R1 = NH2, NH-alkyl, dialkylN, morpholino, or morpholino substituted with 1-2 Me and/or methoxymethyl groups, thiomorpholino, 1,1-dioxothiomorpholino, 2-, 3-, 4-pyridyl, 4-methylpiperazinyl; R2 = H, alkyl, Ph, or R2 together with (CH2)m wherein m = 1, and the intermediate C, N, and O atoms forms an isoxazolyl, 4,5-dihydroisoxazolyl; R3, R4 = H, Me; or R3R4 = O], were prepared Thus, (2R)-1-[3,5-bis(trifluoromethyl)benzoyl]-1-(1H-indol-3-ylmethyl)-4-(2-propanon-1-yl)piperazine, O-[2-

II

Ι

(dimethylamino)ethyl]hydroxylamine dihydrochloride, and NaOAc were refluxed together for 2 h in MeOH to give >95% title compound (II). Several I are said to be active in the neurokinin-agonist induced gerbil foot tapping assay.

RE.CNT 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

- L3 ANSWER 2 OF 10 CAPLUS COPYRIGHT 2004 ACS on STN
- AN 2002:87194 CAPLUS
- DN 136:134787
- TI N-Triazolylmethylpiperazine derivatives as neurokinin receptor antagonists
- IN Jasserand, Daniel; Schoen, Uwe; Sann, Holger; Brueckner, Reinhard; Eeckhout, Christian
- PA Solvay Pharmaceuticals G.m.b.H., Germany
- SO Eur. Pat. Appl., 26 pp.

CODEN: EPXXDW

DT Patent

LA German

FAN.CNT 1

FAN.	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE		
ΡI	EP 1176144 EP 1176144		20020130	EP 2001-117433	20010719		
	R: AT, BE, CH, IE, SI, LT,			, GR, IT, LI, LU, NI	, SE, MC, PT,		
				DE 2000-10036818	A 20000728		
	DE 10036818		20020207	DE 2000-10036818	20000728		
	CN 1335316	A	20020213	CN 2001-122826	20010710		
	•			DE 2000-10036818	A 20000728		
	ZA 2001005737	A	20020122	ZA 2001-5737	20010712		
	!			DE 2000-10036818	A 20000728		
	NZ 513041	A	20021220	NZ 2001-513041	20010718		
	·			DE 2000-10036818	A 20000728		
	AT 244716	\mathbf{E}	20030715	AT 2001-117433	20010719		
				DE 2000-10036818	A 20000728		
	PT 1176144	T	20031128	PT 2001-117433	20010719		
				DE 2000-10036818	A 20000728		
	ES 2201007	Т3	20040316	ES 2001-1117433	20010719		
				DE 2000-10036818	A 20000728		
	JP 2002053577	A2	20020219	JP 2001-224792	20010725		
				DE 2000-10036818	A 20000728		
	CA 2354213	AA	20020128	CA 2001-2354213	20010726		
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			•	DE 2000-10036818	A 20000728		
	NO 2001003709	Α	20020129	NO 2001-3709	20010727		
	•			DE 2000-10036818	A 20000728		
	US 2002065276	A1	20020530	US 2001-915558	20010727		
	US 6407106		20020618				
				DE 2000-10036818	A 20000728		

OS MARPAT 136:134787

RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)

(preparation of N-triazolylmethylpiperazine derivs. as neurokinin receptor antagonists)

IT 393101-98-9P 393102-02-8P 393102-04-0P

RN 393101-98-9 CAPLUS

CN Piperazine, 1-[3,5-bis(trifluoromethyl)benzoyl]-2-(1H-indol-3-ylmethyl)-4-

[[5-(4-morpholinylmethyl)-2H-1,2,3-triazol-4-yl]methyl]-, (2R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

PAGE 1-A

PAGE 2-A

RN 393102-02-8 CAPLUS

CN Piperazine, 1-[3,5-bis(trifluoromethyl)benzoyl]-2-[(1-methyl-1H-indol-3-yl)methyl]-4-[[5-(4-morpholinylmethyl)-2H-1,2,3-triazol-4-yl]methyl]-, (2R)- (9CI) (CA INDEX NAME)

PAGE 1-A

PAGE 2-A

RN 393102-04-0 CAPLUS

CN Piperazine, 1-[3,5-bis(trifluoromethyl)benzoyl]-4-[[5-[(dimethylamino)methyl]-2H-1,2,3-triazol-4-yl]methyl]-2-(1H-indol-3-ylmethyl)-, (2R)- (9CI) (CA INDEX NAME)

IT 393102-00-6P 393102-06-2P 393102-08-4P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of N-triazolylmethylpiperazine derivs. as neurokinin receptor antagonists)

RN 393102-00-6 CAPLUS

CN Piperazine, 1-[3,5-bis(trifluoromethyl)benzoyl]-2-(1H-indol-3-ylmethyl)-4[[5-(1-piperazinylmethyl)-2H-1,2,3-triazol-4-yl]methyl]-, (2R)- (9CI) (CA
INDEX NAME)

PAGE 2-A

RN 393102-06-2 CAPLUS

CN Piperazine, 1-[3,5-bis(trifluoromethyl)benzoyl]-4-[[5-[(diethylamino)methyl]-2H-1,2,3-triazol-4-yl]methyl]-2-(1H-indol-3-ylmethyl)-, (2R)- (9CI) (CA INDEX NAME)

RN 393102-08-4 CAPLUS

CN Piperazine, 4-[[5-[[bis(1-methylethyl)amino]methyl]-2H-1,2,3-triazol-4-yl]methyl]-1-[3,5-bis(trifluoromethyl)benzoyl]-2-(1H-indol-3-ylmethyl)-, (2R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

IT 393102-21-1P 393102-23-3P 393183-40-9P

RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of N-triazolylmethylpiperazine derivs. as neurokinin receptor antagonists)

RN 393102-21-1 CAPLUS

CN Piperazine, 1-[3,5-bis(trifluoromethyl)benzoyl]-2-[(1-methyl-1H-indol-3-yl)methyl]-4-[[5-(4-morpholinylmethyl)-2H-1,2,3-triazol-4-yl]methyl]-, dihydrochloride, (2R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A

PAGE 2-A

•2 HCl

RN 393102-23-3 CAPLUS

CN Piperazine, 1-[3,5-bis(trifluoromethyl)benzoyl]-4-[[5-[(dimethylamino)methyl]-2H-1,2,3-triazol-4-yl]methyl]-2-(1H-indol-3-ylmethyl)-, dihydrochloride, (2R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

<12/2/2004>

Patel

RN 393183-40-9 CAPLUS

CN Piperazine, 1-[3,5-bis(trifluoromethyl)benzoyl]-2-(1H-indol-3-ylmethyl)-4[[5-(4-morpholinylmethyl)-2H-1,2,3-triazol-4-yl]methyl]-, dihydrochloride,
(2R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

PAGE 2-A

●2 HCl

GI

Triazolylmethylpiperazines I [R1 = H, alkyl; R2, R3 = (un)substituted alkyl, cycloalkyl; NR2R3 = (un)substituted heterocyclic]were prepared for use as NK-1 receptor antagonists. Thus, (2R)-I [R1 = H, NR2R3 = morpholino] was prepared by treating (2R)-1-[3,5-bis(trifluoromethyl)benzoyl]-2-(1H-indol-3-ylmethyl)piperazine with C1CH2C.tplbond.CCH2Cl, followed by conversion to the azide, and treatment with morpholine. This compound had pEC50 for NK-1 antagonism in isolated guinea pig aorta.

Ι

RE.CNT 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

- L3 ANSWER 3 OF 10 CAPLUS COPYRIGHT 2004 ACS on STN
- AN 2001:923793 CAPLUS
- DN 136:53766
- TI Process for the preparation of a piperazine derivative as neurokinin antagonist
- IN Koga, Keiichi; Orii, Ryoki; Fujii, Yosuke; Goto, Shunsuke; Hirabayashi, Satoshi
- PA Fujisawa Pharmaceutical Co., Ltd., Japan
- SO PCT Int. Appl., 26 pp. CODEN: PIXXD2
- DT Patent

<12/2/2004>

Patel

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Japanese
FAN.CNT 1
                        KIND
                               DATE
                                           APPLICATION NO.
    PATENT NO.
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                                          WO 2001-JP4884
                                                                  20010608
PΙ
    WO 2001096332
                         A1
                                20011220
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             CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR,
             HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU,
             LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD,
             SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU,
             ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
         RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,
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                                           EP 2001-938576
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             IE, SI, LT, LV, FI, RO, MK, CY, AL, TR
                                            JP 2000-176210
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                                            WO 2001-JP4884
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     US 2003153753
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                                            JP 2000-176210
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                                                                  20010608
                                           WO 2001-JP4884
OS
     CASREACT 136:53766
IT
     381223-96-7P
     RL: IMF (Industrial manufacture); PRP (Properties); SPN (Synthetic
     preparation); THU (Therapeutic use); BIOL (Biological study); PREP
     (Preparation); USES (Uses)
        (process for preparation of piperazine derivative as neurokinin antagonist)
RN
     381223-96-7 CAPLUS
     Piperazine, 1-[3,5-bis(trifluoromethyl)benzoyl]-2-[(3-hydroxy-4-
CN
     methylphenyl)methyl]-4-[2-[(2S)-2-(methoxymethyl)-4-morpholinyl]ethyl]-,
     dihydrochloride, hydrate (2:3), (2R)- (9CI) (CA INDEX NAME)
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Absolute stereochemistry. Rotation (-).

PAGE 1-A

●2 HCl

PAGE 2-A

●3/2 H₂O

IT 277299-25-9P

RN

RL: IMF (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent) (process for preparation of piperazine derivative as neurokinin antagonist) 277299-25-9 CAPLUS

CN Piperazine, 1-[3,5-bis(trifluoromethyl)benzoyl]-2-[(3-hydroxy-4-methylphenyl)methyl]-4-[2-[(2S)-2-(methoxymethyl)-4-morpholinyl]ethyl]-, (2R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

IT 276857-18-2P

RL: IMF (Industrial manufacture); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(process for preparation of piperazine derivative as neurokinin antagonist) 276857-18-2 CAPLUS

RNPiperazine, 1-[3,5-bis(trifluoromethyl)benzoyl]-2-[(3-hydroxy-4-CN methylphenyl) methyl] -4-[2-[(2S)-2-(methoxymethyl)-4-morpholinyl]ethyl]-, dihydrochloride, (2R) - (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

●2 HCl

- (2R) -1-[3,5-Bis(trifluoromethyl)benzoyl]-4-[2-[(2S)-2-AB (methoxymethyl)morpholino]ethyl]-2-(3-hydroxy-4-methylbenzyl)piperazine dihydrochloride, useful as neurokinin antagonist (no data), is prepared from (2R) -4-benzyl-1-[3,5-bis(trifluoromethyl)benzoyl]-2-(3-hydroxy-4methylbenzyl)piperazine via debenzylation, N-alkylation, and conversion into hydrochloride.
- THERE ARE 55 CITED REFERENCES AVAILABLE FOR THIS RECORD RE.CNT 55 ALL CITATIONS AVAILABLE IN THE RE FORMAT
- ANSWER 4 OF 10 CAPLUS COPYRIGHT 2004 ACS on STN L3
- 2000:641466 CAPLUS AN
- DN 133:350193
- TI Non-amide-based combinatorial libraries derived from N-BOC-iminodiacetic acid: solution-phase synthesis of piperazinone libraries with activity against LEF-1/β-catenin-mediated transcription
- Boger, Dale L.; Goldberg, Joel; Satoh, Shigeki; Ambroise, Yves; Cohen, UA Steven B.; Vogt, Peter K.
- Department of Chemistry and The Skaggs Institute for Chemical Biology, The CS Scripps Research Institute, La Jolla, CA, 92037, USA
- Helvetica Chimica Acta (2000), 83(8), 1825-1845 SO CODEN: HCACAV; ISSN: 0018-019X
- PB Verlag Helvetica Chimica Acta
- DTJournal
- LA English
- IT 305325-55-7P 305325-56-8P 305325-57-9P

Patel

RN

CN

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)

(preparation of non-amide-based combinatorial libraries derived from N-BOC-iminodiacetic acid and solution-phase synthesis of piperazinone libraries with activity against lymphoid-enhancer factor-1/ β -catenin-mediated transcription)

305325-55-7 CAPLUS

Piperazinone, 1-(2-furanylmethyl)-4-(4-methoxybenzoyl)-6-(phenylmethyl)-(9CI) (CA INDEX NAME)

$$\begin{array}{c|c}
 & O \\
 & O \\$$

RN 305325-56-8 CAPLUS

CN Piperazinone, 1-(2-furanylmethyl)-4-(4-methylbenzoyl)-6-(phenylmethyl)-(9CI) (CA INDEX NAME)

$$\begin{array}{c|c} O & O & Me \\ \hline O & O & Me \\$$

RN 305325-57-9 CAPLUS

CN Piperazinone, 4-(4-chlorobenzoyl)-1-(2-furanylmethyl)-6-(phenylmethyl)-(9CI) (CA INDEX NAME)

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The development of a solution-phase approach to the rapid, parallel synthesis of highly functionalized piperazinones in only four steps starting from N-BOC-iminodiacetic acid is detailed. The efforts represent the extension of the solution-phase synthesis of combinatorial libraries from N-BOC-iminodiacetic acid to non-amide-based libraries where simple liquid-liquid extns. are employed to purify all reaction products. This methodol. was applied to the synthesis of a diverse 150-member library

with substituents in three positions of the piperazinone core. Screening results from a luciferase reporter assay indicate that a number of library members are novel repressors of LEF-1/ β -catenin-mediated transcription, and may be effective agents against colorectal tumors. Two secondary libraries (100 members each) designed from these lead structures were synthesized and screened, providing addnl. active agents and insight into key structure-activity relationships in the series. These compds. represent only the second class of small mols. which repress transcription of reporter genes containing LEF-1 responsive elements, and the first group not based on DNA minor-groove-binding agents.

RE.CNT 49 THERE ARE 49 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

- L3 ANSWER 5 OF 10 CAPLUS COPYRIGHT 2004 ACS on STN
- AN 2000:421138 CAPLUS
- DN 133:58814
- TI Preparation of piperazines for treating or preventing tachykinin-mediated diseases
- IN Take, Kazuhiko; Konishi, Nobukiyo; Shigenaga, Shinji; Kayakiri, Natsuko; Azami, Hidenori; Eikyu, Yoshiteru; Nakai, Kazuo; Ishida, Junya; Morita, Masataka
- PA Fujisawa Pharmaceutical Co., Ltd., Japan
- SO PCT Int. Appl., 245 pp.

CODEN: PIXXD2

DT Patent

LA English

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				ΑU	1998-7706	Α	19981214
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				WO	1999-JP6943	W	19991210
JP	2003238563	A2	20030827	JP	2003-23481		19991210
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				AU	1998-7706	Α	19981214
				AU	1999-3568	Α	19991021
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				AU	1999-3568	Α	19991021
ZA	2001004597	A	20020905	zA	2001-4597		20010605
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OS MARPAT 133:58814

IT 276857-11-5P 276857-18-2P 276857-20-6P 276858-29-8P 276858-67-4P 276858-84-5P 276858-90-3P 276859-60-0P 276859-61-1P 276859-62-2P 276859-63-3P 276859-64-4P 276859-70-2P 276859-85-9P 276860-42-5P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)

(preparation of piperazines for treating or preventing tachykinin-mediated diseases)

RN 276857-11-5 CAPLUS

CN Piperazine, 1-[3,5-bis(trifluoromethyl)benzoyl]-2-[[3-[(2-methoxyethoxy)methoxy]-4-methylphenyl]methyl]-4-[2-[(3R)-3-(methoxymethyl)-4-morpholinyl]ethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 276857-18-2 CAPLUS

CN Piperazine, 1-[3,5-bis(trifluoromethyl)benzoyl]-2-[(3-hydroxy-4-methylphenyl)methyl]-4-[2-[(2S)-2-(methoxymethyl)-4-morpholinyl]ethyl]-, dihydrochloride, (2R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

●2 HCl

RN 276857-20-6 CAPLUS

CN Piperazine, 1-[3,5-bis(trifluoromethyl)benzoyl]-2-[[3-[(2-methoxyethoxy)methoxy]-4-methylphenyl]methyl]-4-[3-(3-pyridinyl)-2-propynyl]- (9CI) (CA INDEX NAME)

RN 276858-29-8 CAPLUS

CN Piperazine, 1-[3,5-bis(trifluoromethyl)benzoyl]-4-[(3-bromo-1,2,4-oxadiazol-5-yl)methyl]-2-[[3-[(2-methoxyethoxy)methoxy]-4-methylphenyl]methyl]-, (2R)- (9CI) (CA INDEX NAME)

RN 276858-67-4 CAPLUS

CN Piperazine, 1-[3,5-bis(trifluoromethyl)benzoyl]-2-[[3-[(2-methoxyethoxy)methoxy]-4-methylphenyl]methyl]-4-[[1-(triphenylmethyl)-1H-pyrazol-4-yl]methyl]-, (2R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

RN 276858-84-5 CAPLUS

CN Piperazine, 1-[3-[(2,5-dimethyl-1H-pyrrol-1-yl)sulfonyl]-5-(trifluoromethyl)benzoyl]-2-[(3-hydroxy-4-methylphenyl)methyl]-4-[2-[(2S)-2-(methoxymethyl)-4-morpholinyl]ethyl]-, (2R)- (9CI) (CA INDEX NAME)

276858-90-3 CAPLUS RN

Piperazine, 1-[3,5-bis(trifluoromethyl)benzoyl]-2-[(3-hydroxy-4-CNmethylphenyl) methyl] -4 - [4 - [(2S) -2 - (methoxymethyl) -4 - morpholinyl] -2 butynyl]-, (2R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

276859-60-0 CAPLUS RNCN

Methanesulfonic acid, trifluoro-, 5-[[(2R)-1-[3,5bis(trifluoromethyl)benzoyl]-4-[2-[(2S)-2-(methoxymethyl)-4morpholinyl]ethyl]-2-piperazinyl]methyl]-2-methylphenyl ester (9CI) INDEX NAME)

RN 276859-61-1 CAPLUS

CN Piperazine, 1-[3,5-bis(trifluoromethyl)benzoyl]-2-[[3-[(diphenylmethylene)amino]-4-methylphenyl]methyl]-4-[2-[(2S)-2-(methoxymethyl)-4-morpholinyl]ethyl]-, (2R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

RN 276859-62-2 CAPLUS

CN Piperazine, 2-[(3-amino-4-methylphenyl)methyl]-1-[3,5-bis(trifluoromethyl)benzoyl]-4-[2-[(2S)-2-(methoxymethyl)-4-morpholinyl]ethyl]-, (2R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

$$\begin{array}{c} \text{Me} \\ \text{Me} \\ \text{S} \\ \text{N} \\ \text{CF}_3 \\ \end{array}$$

RN 276859-63-3 CAPLUS

CN Piperazine, 2-[(3-amino-4-methylphenyl)methyl]-1-[3,5-bis(trifluoromethyl)benzoyl]-4-[2-[(2S)-2-(methoxymethyl)-4-morpholinyl]ethyl]-, trihydrochloride, (2R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

●3 HCl

RN 276859-64-4 CAPLUS

CN Piperazine, 1-[3,5-bis(trifluoromethyl)benzoyl]-2-[[3-[[(2,5-dioxo-1-pyrrolidinyl)methyl]amino]-4-methylphenyl]methyl]-4-[2-[(2S)-2-(methoxymethyl)-4-morpholinyl]ethyl]-, (2R)- (9CI) (CA INDEX NAME)

RN 276859-70-2 CAPLUS

CN Acetamide, N-[5-[[(2R)-1-[3,5-bis(trifluoromethyl)benzoyl]-4-[2-[(2S)-2-(methoxymethyl)-4-morpholinyl]ethyl]-2-piperazinyl]methyl]-2-methylphenyl]-2,2,2-trifluoro-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 276859-85-9 CAPLUS

CN Benzoic acid, 4-[[(2R)-1-[3,5-bis(trifluoromethyl)benzoyl]-4-[2-[(2S)-2-(methoxymethyl)-4-morpholinyl]ethyl]-2-piperazinyl]methyl]-2-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-, methyl ester (9CI) (CA INDEX NAME)

RN 276860-42-5 CAPLUS

CN Piperazine, 1-[3,5-bis(trifluoromethyl)benzoyl]-2-[[3-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-4-(1-hydroxy-1-methylethyl)phenyl]methyl]-4-[2-[(2S)-2-(methoxymethyl)-4-morpholinyl]ethyl]-, (2R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

IT 276857-12-6P 276857-13-7P 276857-14-8P 276857-15-9P 276857-16-0P 276857-17-1P 276857-19-3P 276857-21-7P 276857-22-8P 276857-23-9P 276857-24-0P 276857-25-1P 276857-26-2P 276857-27-3P 276857-28-4P 276857-32-0P 276857-30-8P 276857-31-9P 276857-35-3P 276857-36-4P 276857-37-5P 276857-38-6P 276857-39-7P 276857-40-0P

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<12/2/2004>

The title compds. [I; Y = bond, alkylene; R1 = (un)substituted aryl; R2 = (un)substituted aryl; R3 = H, alkyl; R4 = (3-pyridyl)alkyl, (3-pyridyl)alkenyl; thiazolylalkyl, etc.] and their pharmaceutically acceptable salts, useful for treating or preventing tachykinin-mediated diseases in human being or animals, were prepared E.g., the piperazine cis-II.2HCl showed more than 80% inhibition of 125I-BH-Substance P binding to h-NK1 receptors at 1 mg/kg, and 100% inhibition of emesis in the dog at 0.32 mg/kg.

RE.CNT 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 6 OF 10 CAPLUS COPYRIGHT 2004 ACS on STN

AN 1999:9836 CAPLUS

DN 130:81525

TI Preparation of aroylpiperazines as tachykinin antagonists.

IN Miyake, Hiroshi; Take, Kazuhiko; Shigenaga, Shinji; Azami, Hidenori; Sasaki, Hiroshi; Eikyu, Yoshiteru; Nakai, Kazuo; Ishida, Junya; Manabe, Takashi; Konishi, Nobukiyo; Terasaka, Tadashi

PA Fujisawa Pharmaceutical Co., Ltd., Japan

SO PCT Int. Appl., 200 pp.

CODEN: PIXXD2

DT Patent

LA English

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WO 1998-JP2613 W 19980615											,	AU :	1997-	7359			A 1	9970	617
											,	WO :	1998-	JP26	13		W 1	9980	615

Page 200 10169415.7

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				WO 1998-JP2613	W	19980615	

MARPAT 130:81525 os

218592-67-7P IT

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses) (preparation of aroylpiperazines as tachykinin antagonists)

218592-67-7 CAPLUS

RNPiperazine, 1-[3,5-bis(trifluoromethyl)benzoyl]-2-[(3,4-CN dimethylphenyl)methyl]-4-(1H-pyrazol-4-ylmethyl)-, (2R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

218592-26-8P 218592-27-9P 218592-28-0P IT 218592-29-1P 218592-30-4P 218592-31-5P 218592-32-6P 218592-33-7P 218592-34-8P 218592-35-9P 218592-36-0P 218592-37-1P 218592-38-2P 218592-39-3P 218592-40-6P 218592-41-7P 218592-45-1P 218592-46-2P 218592-47-3P 218592-48-4P 218592-49-5P 218592-50-8P 218592-51-9P 218592-52-0P 218592-53-1P 218592-54-2P 218592-55-3P 218592-56-4P 218592-58-6P 218592-64-4P

$$\mathbb{R}^{1}$$
 \mathbb{R}^{3}
 \mathbb{R}^{4}
 \mathbb{R}^{2}
 \mathbb{R}^{2}
 \mathbb{R}^{3}
 \mathbb{R}^{4}

The invention relates to the compound I, compds. II, their salts, a process for their preparation, pharmaceuticals comprising them, and their use as medicaments [wherein R1 = trihaloalkyl; R2 = trihaloalkyl; R3 = indolylalkyl; A = CH2 or COCH2; R4 = (un)substituted aminothiazolyl, aminopyridinyl, or 1,2,4-thiadiazolyl]. I and II exhibit tachykinin antagonism, especially antagonism of substance P, and neurokinins A and B. For example, (2R)-1-[3,5-bis(trifluoromethyl)benzoyl]-2-(1H-indol-3-ylmethyl)piperazine (prepared in 6 steps) underwent a sequence of (1) N-alkylation with BrCH2CO2CH2Ph, (2) hydrogenolysis of the ester to the acid, (3) amidation using EDC and HOBt, and (4) salification with fumaric acid, to give title compound I as the fumarate salt (III). In a test for inhibition of 125I-BH-substance P binding to h-NK1 receptors, III gave >90% inhibition at 0.1 μg/mL.

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L3 ANSWER 9 OF 10 CAPLUS COPYRIGHT 2004 ACS on STN
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AN 1997:80506 CAPLUS

DN 126:104102

TI Piperazine derivatives useful as tachykinin antagonists.

IN Matsuo, Masaaki; Hagiwara, Daijiro; Manabe, Takashi; Konishi, Nobuyiko; Shigenaga, Shinji; Murano, Kenji; Matsuda, Hiroshi; Miyake, Hiroshi

PA Fujisawa Pharmaceutical Co., Ltd., Japan

SO PCT Int. Appl., 44 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

PΙ

PATENT NO.	KIND DATE	APPLICATION NO.	DATE
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W: JP, US	•		
RW: AT, BE, CH,	DE, DK, ES, FI,	FR, GB, GR, IE, IT,	LU, MC, NL, PT, SE
		GB 1995-10600	A 19950525
EP 828730	A1 19980318	EP 1996-915199	19960521
R: AT, BE, CH,	DE, DK, ES, FR,	GB, GR, IT, LI, LU,	
		GB 1995-10600	A 19950525
		WO 1996-JP1334	W 19960521

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			GB 1995-10600	Α	19950525
			WO 1996-JP1334	W	19960521

OS MARPAT 126:104102

IT 185750-92-9P 185750-95-2P 185751-01-3P

185751-04-6P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of piperazine derivs. as tachykinin antagonists)

RN 185750-92-9 CAPLUS

CN 1H-1,4-Diazepine, 1-[[4-[3,5-bis(trifluoromethyl)benzoyl]-5-(1H-indol-3-ylmethyl)-2-oxo-1-piperazinyl]acetyl]hexahydro-4-methyl-, monohydrochloride, (R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

● HCl

RN 185750-95-2 CAPLUS

CN Piperazinone, 1-(2-[1,4'-bipiperidin]-1'-yl-2-oxoethyl)-4-[3,5-bis(trifluoromethyl)benzoyl]-5-(1H-indol-3-ylmethyl)-, monohydrochloride, (R)-(9CI) (CA INDEX NAME)

● HCl

RN 185751-01-3 CAPLUS

CN Piperazinone, 1-(4-[1,4'-bipiperidin]-1'-yl-4-oxobutyl)-4-[3,5-bis(trifluoromethyl)benzoyl]-5-(1H-indol-3-ylmethyl)-, monohydrochloride, (R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

$$\begin{array}{c} H \\ N \\ \end{array}$$

$$\begin{array}{c} CF_3 \\ \end{array}$$

$$\begin{array}{c} CF_3 \\ \end{array}$$

● HCl

RN 185751-04-6 CAPLUS

CN 1H-1,4-Diazepine, 1-[4-[4-[3,5-bis(trifluoromethyl)benzoyl]-5-(1H-indol-3-ylmethyl)-2-oxo-1-piperazinyl]-1-oxobutyl]hexahydro-4-methyl-, monohydrochloride, (R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

$$\begin{array}{c} H \\ N \\ O \\ CF_3 \end{array}$$

HCl

GΙ

The invention relates to piperazine derivs. I and their pharmaceutically acceptable salts [wherein A, Y = bond, alkylene; R1 = haloalkyl; R2 = (un)substituted indolyl; Z = H, (un)protected CO2H, (un)substituted or derivatized or (hetero)cyclic carbamoyl; n= 0-2]. The invention also relates to processes for preparation of I, to pharmaceutical compns. comprising them, and to their use for treatment of tachykinin-mediated diseases. For instance, cyclization of (1R)-N2-(bromoacetyl)-N2-[3-

<12/2/2004>

Patel

ANSWER 10 OF 10 CAPLUS COPYRIGHT 2004 ACS on STN

1995:884027 CAPLUS ИA

DN 123:286083

Preparation of piperazine-derivative tachykinin antagonists TI

Matsuo, Masaaki; Hagiwara, Daijiro; Manabe, Takashi; Nobukiyo, Konishi; Shigenaga, Shinji; Murano, Kenji; Matsuda, Hiroshi; Miyake, Hiroshi IN

PΑ Fujisawa Pharmaceutical Co., Ltd., Japan

SO Eur. Pat. Appl., 114 pp.

CODEN: EPXXDW

DTPatent

LA English

FAN.	PA				KIND		DATE		AP:	PLICATION NO.	DATE		
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									GB	1994-2010	A	19940202	
									· GB	1994-12708	A	19940624	
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JP 07242641

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	CN JP JP ZA IL TW	R: AT, 1191533 1072220 11505830 3071829 9604101 118369 391960	BE,		DE, A B T2 B2 A A1		1998 ES, 1998 2001 1999 2000 1996 2000	0610 FR, 0826 1003 0525 0731 0729 0601	WO EP GB, G: US WO CN US JP US WO ZA US IL US TW US GB	1996-JP13 1996-9152 R, IT, LI, 1995-4501 1996-JP13 1996-5355 1995-4501 1996-JP13 1996-4101 1996-4103 1996-4501 1996-4501 1996-8510 1996-8510 1997-8840	335 200 , LU, NL 176 335 744 176 335 176 369 176 06105 176 039	A W A A A A	19960521 19960521 E, PT, IE, 19950525 19960521 19950525 19960521 19950525 19960521 19950525 19960522 19950525 19960522 19950525 19960523 19950525	FI

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     study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use);
     BIOL (Biological study); PREP (Preparation); USES (Uses)
        (preparation of piperazine-derivative tachykinin antagonists)
     169459-14-7 CAPLUS
RN
     Piperazine, 1-[3,5-bis(trifluoromethyl)benzoyl]-4-[2-(1H-indol-2-yl)ethyl]-
CN
     2-(phenylmethyl)-, monohydrochloride, (R)- (9CI) (CA INDEX NAME)
```

Absolute stereochemistry.

● HCl

RN 169459-18-1 CAPLUS

CN Piperazine, 1-[3,5-bis(trifluoromethyl)benzoyl]-4-[3-(1H-indol-2-yl)propyl]-2-(phenylmethyl)-, monohydrochloride, (R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

HCl

RN 169459-22-7 CAPLUS

CN Piperazine, 1-[3,5-bis(trifluoromethyl)benzoyl]-2-(phenylmethyl)-4-(3-pyridinylmethyl)-, dihydrochloride, (R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

●2 HCl

RN 169459-26-1 CAPLUS

CN Piperazine, 1-[3,5-bis(trifluoromethyl)benzoyl]-4-(1H-indol-3-ylacetyl)-2-(phenylmethyl)-, (R)- (9CI) (CA INDEX NAME)

RN 169459-35-2 CAPLUS

CN Piperazine, 1-[3,5-bis(trifluoromethyl)benzoyl]-4-(1H-indol-3-ylcarbonyl)-2-(phenylmethyl)-, (R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 169459-36-3 CAPLUS

CN Piperazine, 1-[3,5-bis(trifluoromethyl)benzoyl]-4-[3-(1H-indol-3-yl)-1-oxopropyl]-2-(phenylmethyl)-, (R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 169459-37-4 CAPLUS

CN Piperazine, 1-[3,5-bis(trifluoromethyl)benzoyl]-4-[4-(1H-indol-3-yl)-1-oxobutyl]-2-(phenylmethyl)-, (R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 169459-41-0 CAPLUS

CN Piperazine, 1-[3,5-bis(trifluoromethyl)benzoyl]-4-[3-(1H-indol-3-yl)-1-oxo-2-propenyl]-2-(phenylmethyl)-, [R-(E)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.

RN 169459-51-2 CAPLUS

CN Piperazine, 1-[3,5-bis(trifluoromethyl)benzoyl]-4-[1-oxo-3-(3-pyridinyl)-2-propenyl]-2-(phenylmethyl)-, [R-(E)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.

RN 169459-52-3 CAPLUS

CN Piperazine, 1-[3,5-bis(trifluoromethyl)benzoyl]-4-[3-(3-furanyl)-1-oxo-2-propenyl]-2-(phenylmethyl)-, [R-(E)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.

RN 169459-56-7 CAPLUS

CN Piperazine, 1-[3,5-bis(trifluoromethyl)benzoyl]-4-[1-oxo-3-(3-thienyl)-2-propenyl]-2-(phenylmethyl)-, [R-(E)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.

RN 169459-57-8 CAPLUS

CN Acetamide, N-[4-[3-[4-[3,5-bis(trifluoromethyl)benzoyl]-3-(phenylmethyl)-1-piperazinyl]-3-oxo-1-propenyl]-2-thiazolyl]-, [R-(E)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.

RN 169459-64-7 CAPLUS

CN Piperazine, 1-[3,5-bis(trifluoromethyl)benzoyl]-2-[(3,4-dimethyl)methyl]-4-[1-oxo-3-(3-pyridinyl)-2-propenyl]-, [R-(E)]-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.

RN 169459-69-2 CAPLUS

CN Piperazine, 1-[3,5-bis(trifluoromethyl)benzoyl]-2-(phenylmethyl)-4-(3-pyridinylacetyl)-, monohydrochloride, (R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

● HCl

RN 169459-70-5 CAPLUS

CN Piperazine, 4-(2-benzofuranylcarbonyl)-1-[3,5-bis(trifluoromethyl)benzoyl]-2-(phenylmethyl)-, (R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 169459-71-6 CAPLUS

CN Piperazine, 1-[3,5-bis(trifluoromethyl)benzoyl]-2-(phenylmethyl)-4-(3-pyridinylcarbonyl)-, monohydrochloride, (R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

• HCl

RN 169459-79-4 CAPLUS

CN Piperazine, 1-[3,5-bis(trifluoromethyl)benzoyl]-2-(1H-indol-3-ylmethyl)-4-(3-pyridinylcarbonyl)-, monohydrochloride, (R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 169459-82-9 CAPLUS

CN Piperazine, 1-[3,5-bis(trifluoromethyl)benzoyl]-2-(1H-indol-3-ylmethyl)-4-[1-oxo-3-(3-pyridinyl)-2-propenyl]-, [R-(E)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.

RN 169459-86-3 CAPLUS

CN Piperazine, 1-[3,5-bis(trifluoromethyl)benzoyl}-2-[(3,4dimethylphenyl)methyl]-4-(3-pyridinylcarbonyl)-, monohydrochloride, (R)(9CI) (CA INDEX NAME)

<12/2/2004>

Absolute stereochemistry.

• HCl

RN 169460-03-1 CAPLUS CN Acetamide, N-[4-[3-[4-[3,5-bis(trifluc

Acetamide, N-[4-[3-[4-[3,5-bis(trifluoromethyl)benzoyl]-3-[(3,4-dimethylphenyl)methyl]-1-piperazinyl]-3-oxo-1-propenyl]-2-thiazolyl]-, [R-(E)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.

RN 169460-04-2 CAPLUS

CN Acetamide, N-[4-[3-[4-[3,5-bis(trifluoromethyl)benzoyl]-3-(1H-indol-3-ylmethyl)-1-piperazinyl]-3-oxo-1-propenyl]-2-thiazolyl]-, [R-(E)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Double bond geometry as shown.

RN 169460-05-3 CAPLUS

CN Piperazine, 1-[3,5-bis(trifluoromethyl)benzoyl]-4-(1H-indol-3-ylmethyl)-2-(phenylmethyl)-, monohydrochloride, (R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

● HCl

RN 169460-11-1 CAPLUS

CN Piperazine, 1-[3,5-bis(trifluoromethyl)benzoyl]-4-[(1-methyl-1H-indol-3-yl)methyl]-2-(phenylmethyl)-, monohydrochloride, (R)- (9CI) (CA INDEX NAME)

● HCl

RN 169460-19-9 CAPLUS
CN Piperazine, 1-[3,5-bis(trifluoromethyl)benzoyl]-2-[(3,4-dimethyl)henyl)methyl]-4-[1-oxo-3-(3-pyridinyl)-2-propenyl]-, monohydrochloride, [R-(E)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.

● HCl

RN 169460-29-1 CAPLUS
CN Piperazine, 1-[3,5-bis(trifluoromethyl)benzoyl]-2-(1H-indol-3-ylmethyl)-4[oxo[4-(triphenylmethyl)-1-piperazinyl]acetyl]-, (R)- (9CI) (CA INDEX NAME)

RN 169460-30-4 CAPLUS
CN Piperazine, 1-[3,5-bis(trifluoromethyl)benzoyl]-4-[3-(1,3-dihydro-1,3-dioxo-2H-isoindol-2-yl)propyl]-2-[(3,4-dimethylphenyl)methyl]-, (R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

• HCl

Absolute stereochemistry.

RN 169460-44-0 CAPLUS
CN Piperazine, 1-[3,5-bis(trifluoromethyl)benzoyl]-2-[(3,4-dimethylphenyl)methyl]-4-[1-oxo-3-(2-thienyl)-2-propenyl]-, [R-(E)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.

RN 169460-45-1 CAPLUS

CN Piperazine, 1-[3,5-bis(trifluoromethyl)benzoyl]-2-(1H-indol-3-ylmethyl)-4-(pyrazinylcarbonyl)-, dihydrochloride, (R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 169460-51-9 CAPLUS

CN Piperazine, 1-[3,5-bis(trifluoromethyl)benzoyl]-2-[(3,4-dimethylphenyl)methyl]-4-(3-pyridinylacetyl)-, (R)- (9CI) (CA INDEX NAME)

RN 169460-52-0 CAPLUS

CN Piperazine, 1-(3,5-dimethylbenzoyl)-2-[(3,4-dimethylphenyl)methyl]-4-[1-oxo-3-(3-pyridinyl)-2-propenyl]-, [R-(E)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.

RN 169460-87-1 CAPLUS

CN 1-Piperazineethanol, 4-[[4-[3,5-bis(trifluoromethyl)benzoyl]-3-(1H-indol-3-ylmethyl)-1-piperazinyl]acetyl]-, dihydrochloride, (R)- (9CI) (CA INDEX NAME)

●2 HC1

RN 169460-88-2 CAPLUS

CN Piperazine, 1-[3,5-bis(trifluoromethyl)benzoyl]-2-(1H-indol-3-ylmethyl)-4[2-oxo-2-[4-(2-pyridinyl)-1-piperazinyl]ethyl]-, trihydrochloride, (R)(9CI) (CA INDEX NAME)

Absolute stereochemistry.

•3 HCl

RN 169460-89-3 CAPLUS

CN Piperazine, 4-[2-(4-acetyl-1-piperazinyl)-2-oxoethyl]-1-[3,5-bis(trifluoromethyl)benzoyl]-2-(1H-indol-3-ylmethyl)-, monohydrochloride, (R)- (9CI) (CA INDEX NAME)

● HCl

RN 169460-90-6 CAPLUS
CN Piperazine, 1-[3,5-bis(trifluoromethyl)benzoyl]-2-(1H-indol-3-ylmethyl)-4[2-oxo-2-(4-phenyl-1-piperazinyl)ethyl]-, dihydrochloride, (R)- (9CI) (CA
INDEX NAME)

Absolute stereochemistry.

●2 HCl

•2 HCl

RN 169460-92-8 CAPLUS

CN Piperazine, 1-[3,5-bis(trifluoromethyl)benzoyl]-4-[2-(4-cyclohexyl-1-piperazinyl)-2-oxoethyl]-2-(1H-indol-3-ylmethyl)-, dihydrochloride, (R)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

•2 HCl

RN 169460-93-9 CAPLUS

CN Piperazine, 1-[3,5-bis(trifluoromethyl)benzoyl]-2-(1H-indol-3-ylmethyl)-4-[2-oxo-2-(4-propyl-1-piperazinyl)ethyl]-, dihydrochloride, (R)- (9CI) (CA INDEX NAME)

Patel

Absolute stereochemistry.

•2 HCl

RN 169460-94-0 CAPLUS

CN 2-Pyrrolidinecarboxamide, 1-[[4-[3,5-bis(trifluoromethyl)benzoyl]-3-(1H-indol-3-ylmethyl)-1-piperazinyl]acetyl]-, monohydrochloride, [S-(R*,S*)]-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

● HCl

RN 169460-95-1 CAPLUS

CN Acetamide, N-[1-[[4-[3,5-bis(trifluoromethyl)benzoyl]-3-(1H-indol-3-ylmethyl)-1-piperazinyl]acetyl]-4-phenyl-4-piperidinyl]-, monohydrochloride, (R)- (9CI) (CA INDEX NAME)

• HCl

RN 169460-96-2 CAPLUS

CN 4-Piperidinecarboxylic acid, 1-[[4-[3,5-bis(trifluoromethyl)benzoyl]-3-(1H-indol-3-ylmethyl)-1-piperazinyl]acetyl]-, ethyl ester, (R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 169460-97-3 CAPLUS

CN Piperazine, 1-[3,5-bis(trifluoromethyl)benzoyl]-2-(1H-indol-3-ylmethyl)-4-[2-oxo-2-(4-oxo-1-piperidinyl)ethyl]-, monohydrochloride, (R)- (9CI) (CA INDEX NAME)

HC1

RN 169460-98-4 CAPLUS

CN 3-Piperidinecarboxamide, 1-[[4-[3,5-bis(trifluoromethyl)benzoyl]-3-(1H-indol-3-ylmethyl)-1-piperazinyl]acetyl]-, monohydrochloride (9CI) (CA INDEX NAME)

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0

● HCl

Absolute stereochemistry.

RN 169461-00-1 CAPLUS
CN Morpholine, 4-[[4-[3,5-bis(trifluoromethyl)benzoyl]-3-[(3,4-dimethylphenyl)methyl]-1-piperazinyl]acetyl]-, monohydrochloride, (R)-(9CI) (CA INDEX NAME)

● HCl

RN 169461-01-2 CAPLUS
CN Acetamide, N-[1-[2-[4-[3,5-bis(trifluoromethyl)benzoyl]-3-[(3,4-dimethylphenyl)methyl]-1-piperazinyl]-2-oxoethyl]-4-phenyl-4-piperidinyl], (R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 169461-02-3 CAPLUS
CN 4-Piperidinecarboxamide, 1-[[4-[3,5-bis(trifluoromethyl)benzoyl]-3-(1H indol-3-ylmethyl)-1-piperazinyl]acetyl]-, monohydrochloride, (R)- (9CI)
 (CA INDEX NAME)

$$\begin{array}{c|c} & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ &$$

● HCl

RN 169461-03-4 CAPLUS

CN 1H-1,4-Diazepine, 1-[[4-[3,5-bis(trifluoromethyl)benzoyl]-3-(1H-indol-3-ylmethyl)-1-piperazinyl]acetyl]hexahydro-4-methyl-, (R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 169461-04-5 CAPLUS

CN Piperazine, 1-[3,5-bis(trifluoromethyl)benzoyl]-4-[2-(4-ethyl-1-piperazinyl)-2-oxoethyl]-2-(1H-indol-3-ylmethyl)-, dihydrochloride, (R)-(9CI) (CA INDEX NAME)

●2 HCl

RN 169461-05-6 CAPLUS
CN Piperazine, 1-[3,5-bis(trifluoromethyl)benzoyl]-2-(1H-indol-3-ylmethyl)-4[2-oxo-2-(1-piperidinyl)ethyl]-, monohydrochloride, (R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

● HCl

RN 169461-06-7 CAPLUS
CN Piperazine, 1-[3,5-bis(trifluoromethyl)benzoyl]-2-(1H-indol-3-ylmethyl)-4[2-oxo-2-(4-phenyl-1-piperidinyl)ethyl]-, monohydrochloride, (R)- (9CI)
(CA INDEX NAME)

HCl

RN 169461-07-8 CAPLUS

CN Piperazine, 1-[3,5-bis(trifluoromethyl)benzoyl]-2-(1H-indol-3-ylmethyl)-4[2-oxo-2-[4-(phenylmethyl)-1-piperidinyl]ethyl]-, monohydrochloride, (R)(9CI) (CA INDEX NAME)

Absolute stereochemistry.

● HCl

RN 169461-08-9 CAPLUS

CN Piperazine, 1-[3,5-bis(trifluoromethyl)benzoyl]-2-(1H-indol-3-ylmethyl)-4-[2-oxo-2-(1-pyrrolidinyl)ethyl]-, monohydrochloride, (R)- (9CI) (CA INDEX NAME)

HC1

RN 169461-09-0 CAPLUS

CN Piperazine, 1-[3,5-bis(trifluoromethyl)benzoyl]-2-(1H-indol-3-ylmethyl)-4-[2-(4-methyl-1-piperazinyl)-2-oxoethyl]-, (R)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 169461-13-6 CAPLUS

CN 1H-1,4-Diazepine, 1-[4-[4-[3,5-bis(trifluoromethyl)benzoyl]-3-(1H-indol-3-ylmethyl)-1-piperazinyl]-1-oxobutyl]hexahydro-4-methyl-, (R)- (9CI) (CA INDEX NAME)

$$(CH_2)_3$$

$$(CF_3)_{Me}$$

RN 169461-17-0 CAPLUS

CN 4-Piperidinecarboxylic acid, 1-[[4-[3,5-bis(trifluoromethyl)benzoyl]-3-(1H-indol-3-ylmethyl)-1-piperazinyl]acetyl]-, monohydrochloride, (R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

● HCl

RN 169461-30-7 CAPLUS

CN Acetamide, N-[4-[4-[3,5-bis(trifluoromethyl)benzoyl]-3-[(3,4-dimethylphenyl)methyl]-1-piperazinyl]methyl]-2-thiazolyl]-, (R)- (9CI) (CA INDEX NAME)

RN

169461-46-5 CAPLUS
Piperazine, 1-[3,5-bis(trifluoromethyl)benzoyl]-2-(1H-indol-3-ylmethyl)-4-CN [2-oxo-2-(1-piperazinyl)ethyl]-, dihydrochloride, (R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

2 HCl

169461-47-6 CAPLUS RN

Piperazine, 1-[3,5-bis(trifluoromethyl)benzoyl]-4-[(1,3-dihydro-1,3-dioxo-CN2H-isoindol-2-yl)acetyl]-2-(1H-indol-3-ylmethyl)-, (R)- (9CI) (CA INDEX NAME)

RN 169461-65-8 CAPLUS

CN Piperazine, 1-[3,4-bis(trifluoromethyl)benzoyl]-4-[3-(1,3-dihydro-1,3-dioxo-2H-isoindol-2-yl)propyl]-2-(1H-indol-3-ylmethyl)-, (R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 169461-66-9 CAPLUS

CN Piperazine, 1-[3,4-bis(trifluoromethyl)benzoyl]-4-[4-(1,3-dihydro-1,3-dioxo-2H-isoindol-2-yl)butyl]-2-(1H-indol-3-ylmethyl)-, (R)- (9CI) (CA INDEX NAME)

RN 169461-78-3 CAPLUS

CN Piperazine, 1-[3,4-bis(trifluoromethyl)benzoyl]-2-(1H-indol-3-ylmethyl)-4-[4-(4-methyl-1-piperazinyl)-4-oxobutyl]-, (R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

$$(CH_2)_3$$

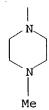
$$(CF_3)_{Me}$$

RN 169461-89-6 CAPLUS

CN Piperazine, 1-[3,4-bis(trifluoromethyl)benzoyl]-2-(1H-indol-3-ylmethyl)-4[1-methyl-2-(4-methyl-1-piperazinyl)-2-oxoethyl]-, monohydrochloride (9CI)
(CA INDEX NAME)

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$$F_3C$$
 CF_3
 CH_2
 PAGE 2-A



● HCl

RN 169461-92-1 CAPLUS
CN 1H-1,4-Diazepine, 1-[[4-[3,4-bis(trifluoromethyl)benzoyl]-3-(1H-indol-3-ylmethyl)-1-piperazinyl]acetyl]hexahydro-4-methyl-, (R)-,
2-hydroxy-1,2,3-propanetricarboxylate (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 169461-91-0 CMF C30 H33 F6 N5 O2

CM 2

CRN 77-92-9 CMF C6 H8 O7

$$\begin{array}{c} {\rm CO_2H} \\ | \\ {\rm HO_2C-CH_2-C-CH_2-CO_2H} \\ | \\ {\rm OH} \end{array}$$

RN 169462-05-9 CAPLUS

CN Piperazine, 1-[3,4-bis(trifluoromethyl)benzoyl]-2-(1H-indol-3-ylmethyl)-4[4-oxo-4-[4-(phenylmethyl)-1-piperazinyl]butyl]-, monohydrochloride, (R)(9CI) (CA INDEX NAME)

Absolute stereochemistry.

● HCl

RN 169462-06-0 CAPLUS

CN Piperazine, 1-[3,4-bis(trifluoromethyl)benzoyl]-2-(1H-indol-3-ylmethyl)-4[4-oxo-4-(4-phenyl-1-piperazinyl)butyl]-, dihydrochloride, (R)- (9CI) (CA
INDEX NAME)

Absolute stereochemistry.

•2 HCl

RN 169462-07-1 CAPLUS

CN Piperazine, 1-[3,4-bis(trifluoromethyl)benzoyl]-4-[4-(4-cyclohexyl-1-piperazinyl)-4-oxobutyl]-2-(1H-indol-3-ylmethyl)-, dihydrochloride, (R)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

●2 HCl

RN 169462-09-3 CAPLUS

Piperazine, 1-[3,4-bis(trifluoromethyl)benzoyl]-2-(1H-indol-3-ylmethyl)-4-CN [4-oxo-4-(1-piperidinyl)butyl]-, monohydrochloride, (R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

● HCl

169462-10-6 CAPLUS RN

Piperazine, 1-[3,4-bis(trifluoromethyl)benzoyl]-2-(1H-indol-3-ylmethyl)-4-CN [4-oxo-4-[4-(2-pyridinyl)-1-piperazinyl]butyl]-, trihydrochloride, (R)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

3 HCl

RN 169462-11-7 CAPLUS

CN Piperazine, 1-[3,4-bis(trifluoromethyl)benzoyl]-2-(1H-indol-3-ylmethyl)-4[4-oxo-4-(4-phenyl-1-piperidinyl)butyl]-, monohydrochloride, (R)- (9CI)
(CA INDEX NAME)

Absolute stereochemistry.

$$\begin{array}{c} H \\ N \\ \end{array}$$

$$\begin{array}{c} CF_3 \\ \end{array}$$

HCl

RN 169462-12-8 CAPLUS

CN Piperazine, 1-[3,4-bis(trifluoromethyl)benzoyl]-2-(1H-indol-3-ylmethyl)-4-[4-oxo-4-[4-(triphenylmethyl)-1-piperazinyl]butyl]-, (R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 169462-13-9 CAPLUS

CN Piperazine, 1-[3,4-bis(trifluoromethyl)benzoyl]-2-(1H-indol-3-ylmethyl)-4-[4-oxo-4-(1-piperazinyl)butyl]-, dihydrochloride, (R)- (9CI) (CA INDEX NAME)

$$\begin{array}{c} H \\ N \\ \end{array}$$

$$\begin{array}{c} CF_3 \\ \end{array}$$

●2 HCl

RN 169462-15-1 CAPLUS

CN 1H-1,4-Diazepine, 1-[4-[4-[3,4-bis(trifluoromethyl)benzoyl]-3-(1H-indol-3-ylmethyl)-1-piperazinyl]-1-oxobutyl]hexahydro-4-methyl-, (R)-, sulfate (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 169462-14-0 CMF C32 H37 F6 N5 O2

Absolute stereochemistry.

$$(CH_2)_3$$

$$(CF_3)_{Me}$$

CM 2

CRN 7664-93-9 CMF H2 O4 S